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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Robert A. Holton et al. Serial No. 09/978,436 Filed October 16, 2001 Confirmation No. 5339 RADIOSENSITIZING TAXANES AND THEIR PHARMACEUTICAL PREPARATIONS For

**ART UNIT 1625** 

DECLARATION OF PRIOR INVENTION UNDER 37 C.F.R. ' 1,131

We, Robert A. Holton, Hossain Nadizadeh and Li-Xi Yang declare as follows:

- We are the inventors of the subject matter claimed in the aboveentitled United States patent application.
- We are submitting this Declaration to establish completion of our 2. invention in the U.S. before June 7, 1995, the filing date of U.S. Patent No. 5,780,653.
- 3. We reduced to practice the invention claimed in this application in the United States before June 7, 1995.
- 4. Facts in support of this Declaration are attached hereto as Exhibit A. Exhibit A is a true and correct copy of experimental note book page numbers 1-6, 8-14, 16, 18, 20, 22-28, 30-38, 40, 42-44, 46, 48, 50, 52, 54-62, 64, 66, 68-74, 76-78, pages 1-4 of "Taxol and TM 24 hrs prior Xray," pages 1-3 of "TM drug,"

pages 1-3 of 'TNB," 'TNB+22Gy" and 'TNB control" (with dates deleted), upon which Figures 1-18 and Examples 4.1, 4.2, 4.4, 4.5, 4.6 of this application are based. Specifically, compound taxol-metro (or TM) corresponds to N-debenzoyl-N-(t-butylcarbamoyl)-7-(metronidazoleoxycarbonyl)taxol of Example 2 and nitrophenyl taxol (or taxol nitrobenzene or TNB) corresponds to N-debenzoyl-N-(t-butylcarbamoyl)-3'-desphenyl-3'-(4-nitrophenyl)taxol of Example 3 of this application. As such, Exhibit A evidences our reduction to practice of the invention claimed in the application prior to June 7, 1995.

5. We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. ' 1001, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Robert A. Holton	4/28/03 Date
Hossain Nadizadeh	Date
Li-Xi Yang	 Date



### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of Robert A. Holton et al. Serial No. 09/978,436 Filed October 16, 2001 Confirmation No. 5339

**ART UNIT 1625** 

FOR RADIOSENSITIZING TAXANES AND THEIR PHARMACEUTICAL PREPARATIONS

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Robert A. Holton	Date
Hossain Nadizadeh	Date
Li-Xi Yang	<u>4/28/03</u> Date

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Robert A. Holton	Date
Mudizadeh  Hossain Nadizadeh	<u>4/28/03</u> Date
Li-Xî Yang	Date

metromagile - Cl. and metromidable - I Toxicity under Or /N'2. 358/g = 4.4 x10 = 1+21 = 2x10 a 0.1 +2.1 = 2x100 1+9 = 2000. 4.++40.5 = 200. Each dish: It all day silution + Drigs: Solvent: Droso metro-12: stack: 1: 1.06M 126,160,151, 0:1457 0.054 77.40°-I 3.54 0.71 0.14 3. metro-cl 7.89 152,151,159 4.75 1.05. 1.00 130,156,124, 156 0.95

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古山田東山田東京大学大学大学大学 地名の一世代

Surviving

Fraction

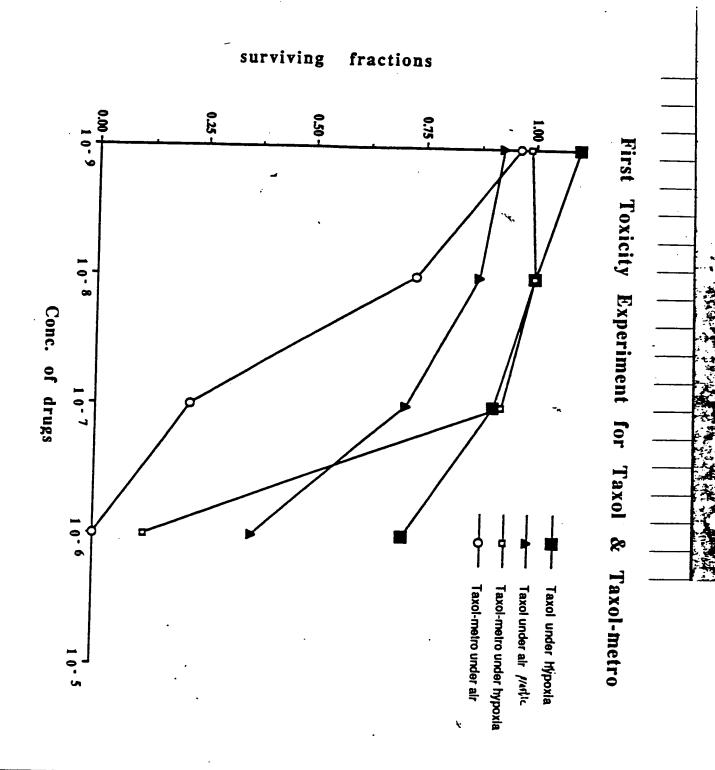
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The Broadway Service Blinds

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	sensitifation of CHO coils By networ	rida II (M-I)
- Augus	W-I: from strik 1.19M., get out me	a diluter with 0.75 ml
_ Dig_	DMSO to make a M-I solution	on of 0.476M, From who
	0.54 mil was teller, alded in	to 7/. send HBss,
	freezing find Conc. of 3.1	-4 mM.
Ting in Rodi	ation (9x). No + Doug. No . (1. + Drug.	
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31 3/C Law	at 48 cm, at 201 rod inside the	ender exist you rad faire.
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4 of 40. 54. 46 0 36. 44. 25	(08)	0.78 (PE)

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and of them.				SFFE
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-8 2dish 140.132 136 0 to 1.0"	112.106	139	0.545	
-7 zdish 13/. 114. 1225 o.6125 o.911	51.60	55.5	0.2775	0.363
-6 7dish 47. 94. 95.5 0.275 0.71	15-9.147	153	0.765 (P	E)
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	- w t b	1.—2. 2. 525 py	رأ مسترات ا	ml = 10-6	
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6	1000	500	4	1666	1000
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		acubator th	,	p /h w	ith chamber incub
24 hr than r		·	_		
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64 B. 196.231	205.3	0.205 0.356	172.175.178	175	0.35 0.486
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C2+ Prug			Cz		
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ly 27. 28. 272	278.3	6.0557 5.098	354.347.352.	351	0.0702 0.102
46f 133. 133.141	137.6.	0.138 0.245	50.286.754	263.3	0.263 0.383
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Radios en itientien	_of (ME(Y-)2N'(CH2)41	N(inetro)z	(4c)	 
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Phated Cell in dish	incubation 2.5h Shop	- and brig	<del></del>	111
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861 0 0	0 0 gz. 14.46	74	0.062 0.168	1/
rif o o	c 0 125.129.120		0.24 6.65	
607 36.8.9 17.7	0.0035 0.024 136. 132. 90	117.3		
767	5.15 (PE) 16.44.82	74_	0.37 (PE)	•
0 47.07.07	: 82		v.023 c.034	Dr.
8/4 704 204 209.	0.0209 0.036 22]. 224	· 232 227.7		
39 25	728 741	311 317.7	0.064 0.08	
Cox C.E. Mu . J	-2 -2 -73	230 216.7	0.47 0.323	
1.2.101.07	0.557 (PE) 118. 130.	155 134.3	0.67 (PE)	
0 165. 120.109 111.3	<u> </u>			
	<u> </u>			<del>_</del>
\			+	
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	and the second second	<del></del>	and the second s	

						·				
•		Taxel and	Tarel-	nitrobe	12:11	e toxicity	,			
	1= Timis!	riz Count	Ir each	_ 55-	55,=	22 court	pi san	SF	SFIFE	
	1-5	71.74.75	27.6	6.41	5.74	4.5.6		6.325	o.vel	
		82.75.71				25.25.19	23	0.115	5.14	
	•	94.93.32					73.7	e.37	vito	
		128. 110.113					129.3	6.65	1.05	
duth.	7-9	105, 106.126	112.3	0.5% 1	307	132.126.119	125.7	0.63	1.02	
	1113 = Taxel	-Mitysbergine								
		0. 0.0				0.0.0	υ	J	U	
		39.49.52					/.3	0.007	0.01	•
	TAB-7	91. 81. 96	84.3	0.447	080	40.19.32	30.3	0.15	0.25	
	TA13-8 8	34. 98. 96	92.7	0.46	0.83	29.29.57	36.3	0.19	0.3/	
	T1B-9 1	02. 92.102.	98.7	0.49	0.88	66.70.50	62	0.31	0.50	
		0.111.114						o. 615 (PE		
	Eash 313	h idd iso	Œ1/. p	not co	:1/ in	dish insu	hater 6 hr	then a	del drug p	1 dem
-	_ if cet _ f'	ivith a	wamper	incubir	م مرده	upr. oxic	in incub	ator.		
ļ	Trug Taxo	1 from Im	120.3	ml +29.	7:-1=	10-5	TNB 1.01	1 -> 0.3n	4+29.74=	10-5
			4+27m	1=10	6			+ 27 m =		
		3~	1 + 27 m	1=10	7:			+27 me =		
			¥ 27 w					12700-		
		<u>3</u>	+ 27 m	=10-9			, ~ . 	ν 	2-9	
_				<del></del>						
		<del></del>	·		: 		·····			
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10.000 2000 -			+ Drug 0,000	10.000
	1		_ <del></del>	
	3'2"	6	5000	5000
1,00	Z',"	4	1600	1000
200			200	200
2.5 for then a	ld ong P"	i mi chu	ofter put u	laterbuth
n incubistor.	Dri	if & Arom	300 IMI=30	
	- <u></u>	10.1	g mil +20 m(=	/mm ·
		8	m + 72 m =	0.1m1 ·
			(Car) (bul	
SFE NZ	Count	mem	55	9 F/PE
		49	0.094	0.017
0.0407 71	. 80. 72.	74.3	0.037	0.073
0.258 132	. 85.79	18.7	0.20	0.39
(PE): 114	. 84.110	102.7	051(PE)	
02				
6 0.992 162	. 52.149.	154.3	0.015	0.027
2 0.064 228	. 235. 231	23/.3	0.046	0.08
	41. 165	157.3	0457	0.27
		15.3	0.58 (PE	:)
	•	p		
	2.5 for then 2 In incubator.  35/pE N2 0.0066 123 0.0407 71 0.258 132 (PE): 114 22 2 0.064 228 7 0.25 166.	2.5 for . then add Drug Pri 2.5 for . then add Drug Pri 2.5 fe Nz Court 0.0066 123. 102.72. 0.0407 71.80.72. 0.258 132.85.79 (PE): 114.84.110 22 20.064 228.235.231 7 0.25 166.441.165 (PE): 104.121.121	2.5/m. then add Drug pumps ihr a incubator.  Trig = from 10.0  8  0.0066 123.102.72. 99  0.0407 71.80.72. 74.3  0.258 132.85.79 18.7  (PE): 114.84.110 102.7  2 0.064 228.235.231 23/.3  7 0.25 166.41.165 157.3  (PE): 124.121 15.3	2.5/or. flee add Drug promps ihr after put when incubator.  Driegt from DP IM = 30 (0.9 ml + 120 ml = 30 (0.9

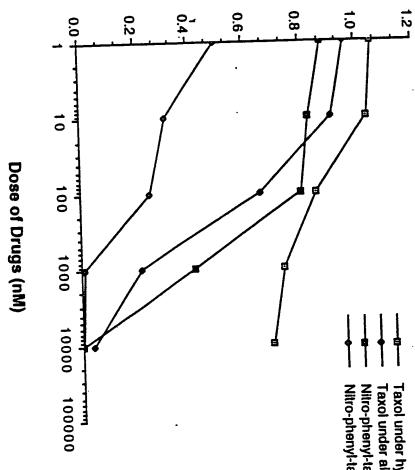
		·		- Estano 12131	1 9.697 mg/	·
DBT	M + Radiation	<i>P P I</i>	37M=4C			
p-	N2+D	Nz Time	(61) 62+D	0.54 m	1+74.46 mil = 1	7.1 mM
18	20,000	10,000	\$ 5000	5600		<del></del>
izay	5000	2000	-6 2000	2000		
<u>.</u>	1000	500	4 1000	1000		
-	740	200	0 700	200		
post ed	cell in dish	2 Clar incuba	to then add	Out Bump	Ihr Ater	pump put
Wint Barbara	th 37°C (hr)	then redication of	ter wash 41 the	drug add new	medium peep	m missign 70001)
		SF 59/0E	Nzant	mean_	SF	SF/PE
N2+Day Com	38.7	0.0019 0.006	101.91.30.	74	0.0074	0.053
47.81.127	<u> </u>	0.017 0.053		61	0.0305	0,22
	94.7	0.095 0.3	29. 22.82	44.3	0.09	0.63
77.83.124		0.32 (PE)	42. 25.15	77.3	0.14 (PE)	
73.32.88	04.)					
0 + Del			02			
Ozt Pruf NA 5372	70	0.014 0.026	104.97.87	96	0.019	0.03
84.53.73	118.3	0.059 0.106		147.3	0.074	0.12
110-129-116	159.7	0.16 0.29	159-173-176	169.3	0.17	0.28
164.154.161	112	0.56(PE)	120.136.110	122	0.61 (PE)	
120.110.106		0.50(1.25)				
,						·
		i				
		<del></del>	,	ŕ.		
						•
	: •• ·	·· <u>- 7,5-0</u> 2				

CTM=5C TOXICA	y Experiment		
1. 101.98	Az 23		
2. 40.106	<u> </u>		
3. 108.124	6.12	· ((CPE)	
120 136. Iso o.	61 (PE) 42.25.15 3.5 hr: nowbator. Feeth dis	h add zoo cells.	
prated cell in dish.	3.5 hr incubacot .	in the the	
	add troy pump ) hr. Wan	iaterimin in .	•
5C = 9.15 m2 + 14.85 m2 (ABS)	)=1 mM. 5C1.		
1. Cul + 13.5 ml HB3	5 = 0.1 mM 5CZ.		
15-1-13.5 mg HBS	S = 0.01 mM 5C3.		
·			*
			· · · · · · · · · · · · · · · · · · ·
			<u> </u>
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		+.	<u> </u>
	•-		

		:			<del></del>		<del></del>
CTM = 5 C + Radiation	<u>n</u>	zdiđi	in a	<u> </u>			<del></del>
G:1) Nz + Drug	N2_		Dz+Privj	<u></u>		· ——— · · · · · · · · · · · · · · · · ·	
(of 20.000	10.000		10.000		5000	<u> </u>	
6f 5000	2000	6_	2000		1000		
66f 1000	500	4	. 1000		500		
0 200	200	0			700		
			Dru	9: from CPM=5C	0.15 ml	+14.85 ml= /m1	<u>M.</u>
		i			0.025n	12 +75 ml = 0/11 HBSS	11
plated cell in dish	2 r l	well bet and	then ald	with gung this	(xul)	HBSS	
			year par	ary / /	7,421-		
waterbuth the 37°C.			SF/PE	Netount	mem	SF-	SF/PE.
N2+0xug Count	mem.	}	/ /	158.125.164	172.3	0.017	0.025
- 38.44.19	33.7	0.0017	·	157.127.119	134.3	0.067	0.099
67 62.72.94	7b	6.0152		154. 155. 173	166.7	0:32	0.47
67 159.143.72	124.7	0.12		176.132.140	136	0.68(PE	
; 109.10g.10g	108.7	5.54(	<i>P=)</i>			0.00(1-	
02+12rug			: :	<u> </u>			1
6\$ 198. 232.215	215	0.0215	6.632	99.113.95	102.3	0.02	0.03
if 140.156.1=9	141.7	0.071	6.106	67.64.80	70.3	(0,0)	0.107
ist 158. 181. 150	163.	5.163	0.24	113.104.99	105.3	6.21	0.319
9 138. 139 124	133.7	0.67 (H	在)	144.124.128	132	0.66(PE)	
, , , , , , , , , , , , , , , , , , , ,							
							!
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			<u> </u>				•

-	1			. –				•
	Lovel	and Taxo	1- nitrob	enzine to	Micity			
		- Commit	i) iiim	SF SF/PE	Oz Court	mean	57-	SFIZE
1-5	dish			c.23.3 5.62 7		7.5	6.0375	0.07
- b	· · ·	46.53		5.2475 c.647		19.5	0.0975	0.17
- V	<u> </u>	95. 93		2.47 1.23	y 72.5	61	6.355	0.53
1-8		74. 73		0 3675 0.46	127.121	124	C.E2	1.08
1-9	<del></del>	30.80		5.4 1.05	. 46.114	155	0.535	C. 41
		74. 79		c.3825 (PE)		115	0.575 (PE	)
0 [185		0 3	2	//		0	9	ی
•		33. Zo	76.5	0.1325 5.35;		2	0.01	<u> </u>
118-6	<u>, , , , , , , , , , , , , , , , , , , </u>	63. 77.	73	c 3825 0.74	2	74.9	c.195	0.48
[NZ-7]		69. 77.	73.	c.365 0.95			0.28	0.49
			81.	0.405 1.cb		87	6.435	0.76
1407	<del></del>	81. 31.	31.	:				
	el. J	1 11 0	all DW	t investor 6	hr. then add	drug. Hypoxi	ic pump Ihr.	then with
Eac	ne ce	an an vo	to all	w orie inco	whator raper.	after worth of	the dong.	
Cha	om bld	pwo jacaa	10-5	- 57.5 BUS	3: 0.2 +19.8 ~	L=10-5		
-Jaac	<i>71:</i>	0.2+19.8=	-h	1700	2ne+18ne	=10-6		
	<u></u>	2n(+18ml=1	-7		zue+18me	= 10 <sup>-7</sup>		
		2ml + 18ml =	-8	İ	me+18n	=10-8		
		ムルチほんこ	10	1_	77-10			

# Surviving Fraction

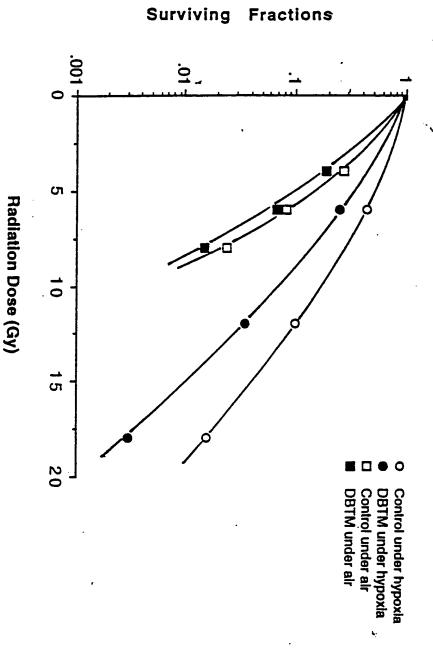


Chemotherapeutic activitiés of Taxol & Nitro-phenyl-taxol against CHO Cells

Taxol under hypoxia
Taxol under air
Nitro-phenyl-taxol under hypoxi
Nitro-phenyl-taxol under air

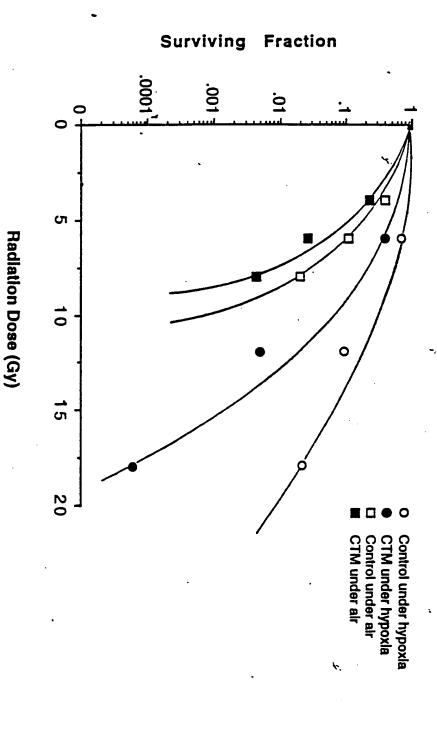
	+ Radiation	n			OB	TM = 0.1 mM	
RT (64) 1/2+D/m/	No	RTI	Oztlory		02		
B 70.600	10200	•	-	<u> </u>	5000		
12 5660	7,000		2000		1000		
h 1000	500	4	1000		500		
0 200	200	ی	200		700		
	Dru	g: from	9.697 mm.				
			.62~l+73.4=0				
posted cell in dig	h 2.5 hring	ubstor	then add di	ref pump	1hr. then	put waterbuth	37°C
1 hr. otic in inci	whater after	Validi.	m				
NZ+12 Court me	en SF	STOF	No Court	mean	SF	SPPE	<del></del> -
164 30.38.29 32.	3 0.0016	وي و د. و	83.86.94	87.7	0.008	0.016	
6f 106. 93.88 45.7			122.109.106		0.056	0.1	
	3 0.157	0.25	131. 126.113	123.3	0.25	0.44	
2 45. 110.98 107.7			120.103.115	112.3	0.56(PE)		
02+0 court		!	Oz Court	·			
864 03.39.43 41.7	0.008	0.015	61.61.58	60	0.0/2	0.024	
66 68.79.72 73	0.0365	0.068	40. 31.49	4z.7	0.043	0.084	
16/ 105.101.97 101	0./0/	0.19	58.74.75	69	0.138	0.27	
0 103.113.110 108.	7 0.54 (PE.	)	15. 95. 14	10/.3	0.51 (PE)		
	:						
		i					
					+		





	A h 0	1. 1.					CTM	=0.1mM		٠
disting	CTM=5C + Rad	iation		RT			62	_ · · <del>-</del>		•
(4)	_Nztoruj			_( <i>OF)</i>	10.00	•	5000			•-
18	20, 500		0.000		200		1000			-
12	5000		C.	<u> 6                                   </u>	1000		500			٠.
6	1000		500				200's			`-
0	200		200	<u> </u>	. 200					
		D,	•	'an 161		: 1 = 1 : A			<del></del>	
				0.076 n	14 75 ( HB)	me = 0./m/)		He cout	Whatabuth	
F	plated cell in	digh i	newleto	3.5	by the	n add drug pa	-p/my.	ala pro	Carrie 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1	~
3	7°C Ilw. Vadiati			Ming in	· jucuba	Toy.	in epa	SF	SF/PE	-1
	N2 + Druf Count	mean		57 5		Nr Court 114. 109.95	106	0.0106	0.022	_
801	(, 0.0.	0.3		0002 0			93	0.0465	0.097	<u> </u>
264	6.7.8			1 <u>4</u> 0.0		83.113.83	<u>73</u> 144.7	0.33	0.69	<u> </u>
but	101.104.123	109.3	0.10		<u> </u>	166.162.166				_
0	68. 45.48	<u>53.7</u>	6-27	(YZ)		100. 88. 99	45.7	0.48 (PE	·)	1
	Cz + Druf Count					02 Count		4	0.02	
364	22.18.16	18.7	0.001	9 0.0	<u>4}</u>	47.42.51	46.7	0.009	0.109	
664	27.16.25	22.7	0.01	9,0	26	35.44.65	48	0.048		7
.,	78. 107.115	100	911	0.2	3	88. 87.90	88.3	0.18	0.4	_
	88-108.63	86.3	043(	PE)		94.82.89	<i>8</i> 8⋅3	0.44 (P.	٤)	
							<u></u>			-
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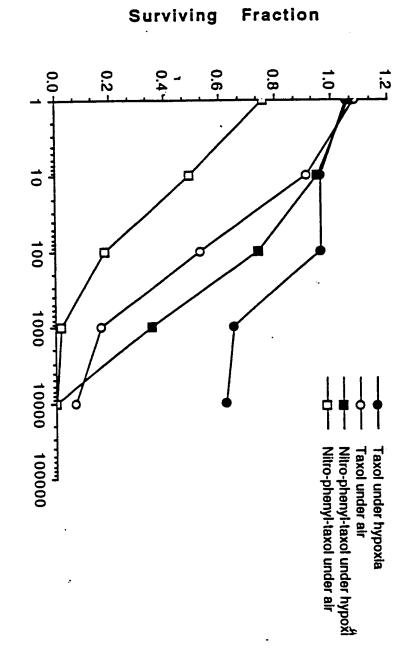


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				CTM	=0.1 m M	<u></u>
CTM=5C + R	adiation	RT	Oztory		Oz	
RT Ne+Dry	N2	RT (Gd)	5000		5000	
18 20.000	10.000		1000		1000	
12 5000	2000	<u>-6</u>	500		500	
1 1000	500	4			200	
0 200	200	0	200			
		<u>: المتال ال</u>	from 100 mm.			
		·	0.076 m 1 + 75 m =	blica.	pot water	with 37° lbr.
parted cell in di	th incubator	3 hr: add	avus purp in	r then	1	
then Vadiation	oxic in in				SF	STIPE
N2+17cy Count	man SF	SPE	N2 Count	<u>тем</u> 150	0.05	0.025
<del></del>	3.3 0.000	17 0.0003	140.145.166		0.0695	
- <del> </del>	26.7 0.005	3 0.01	151.166.121	139	0.31	0.5
1707 13.4	112.3 0.112	0.26	144.158.58	153.3	0.51 0.608(P	
603 174.11		2(PE):	123. 110.132	14.7	61008[1	
0 11		:	02 count			0.03
5 21 02 10 104	106.7 0.0	2 0.03	121.117.107	15	0.023	0.095
63 863 10.110.11		73 0.114.	61.76.57	64.7	0.065	0.35
1661 01 20 0		25 0.35	122.121.111	118		<del></del>
64 126.104.107		Q (PE)	138.135.135	136	0.68 (P	·
0 124. 140.121	160.7			· 		
						·
		<del>-</del>				

Texto L and	Taxol nitrobenzine roticity  SFJE 02 maan SF SFJE
Nz_ Mzan	5F
-5 12.16	
c6 29.21	9-4
c7 74.105	80.70
7-8 79.74	147.14
7-9 111.89	117.127
0 120.106	130.10
[NB5 0 0	. 00
(a13-6 33.33	1.4
11B-7 81·73	24.36
18-8 84.44	56.82
113-9 90.120	\$5.53
	1= Taxo   TNB = Taxol nitrobenzine
each digh plant	ed zoo cells in incurator 6hr. that add drug hypoxic pump lbr.
Than with cham	ber put incubator 24 hr. oxicade duy incubator 24 hr.
Drug from: Tan	10: 0:2 ml + 198 ml = 10-5 TNB: 22 ml + 19.8 ml = 10-5
	Zne +18m2-10
•	2ml + (fund = 10
•	7. 4 + 18 = 10-1 2nd + 18 ml = 10-4
•	2m+18ml=10-9 2ml +18ml =10-9
•	
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	the state of the s

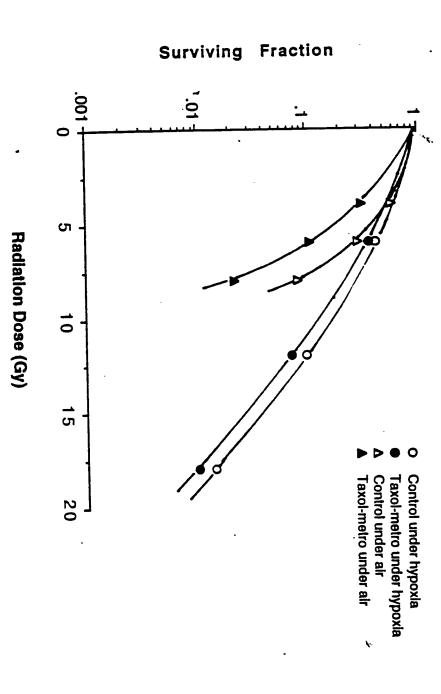
# Chemotherapeutic Activities of Taxol & Nitro-phenyl-taxol against CHO Cells



Dose of Drugs (nM)

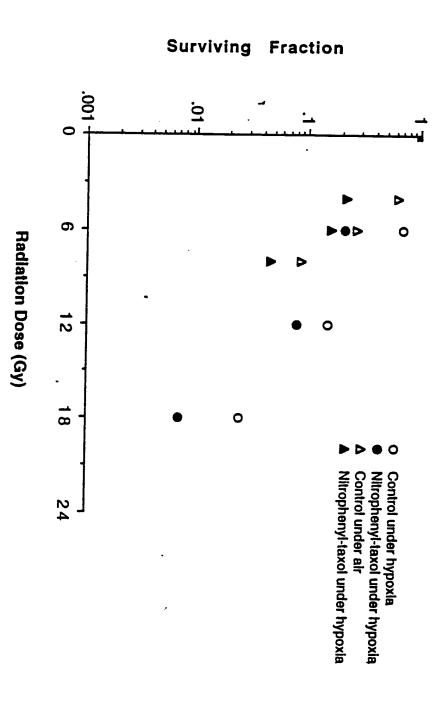
-[2401-meter t	Radiation_	(2+7) wh	02			
RT RT 12+Dieg	1/2 (4)	5000	200	<u> </u>		· •
18 70.666	10.660	7200	1000	, 		<b>†</b>
12 5063	2000 B	1660	500			
6 (000	Z00 C	7.5 <i>0</i>	250			
0 200	1 / / / / / / / / / / / / / / / / / / /	then add and E		Thic in incu	ebate 1	-
photod cell in dish inc	unally sur	tor zet lw. the	~ vadiation.			+-
after pump with champ	Disch	. Taxol-motto im	Μ			+
	7	1.45:nl =10-5 (medialm)		7		+-
		(medialm)	7 (oml +9	30ml=10-/	cr/	+
	SE SHE	N2 Count	M Gan	<u> 5</u> F	STPE	+
1 No +1) Count 111 Pm	7, 1	118. 26. 84.	49.3	0.0099	0.014	+
1/6/ 110.139.15 121.3	-1	129.164.57	143.}	6.072	0.1	+
-1264 216.227.209 217.3	<u> </u>	152.167.138	152.3	0.3	0.427	-
- for 178. 237. 229 215.3	0.215 6.385 6.59 (PE)	139. 147. 138	141.3	0.71 (PE	) 57/pz	+
- p 126. (03.126 118.3	57 5F	Cont	med	SF		+
- Cz + Dyig Const 111800			121.3	0.06	0.085	+
- 15 12. 16.12. 13.3	0.0xf 0.1	214. 207. 226	215.7	0.216	0.3	+
66 25. 27. 30 27.3	0.039 0.32		7 214	c.428	0.549	十
40 31. 35. 50 38.7	0.017 035	143. 13f. 14f	143	6.715 (F	E)	1
<u>v 24.27.23 24.7</u>	512 (PÉ)					一
						1
		•	# #			-1
						$\dashv$
	:				<del> </del>	-
	<del></del> :					





72 Yo - nitrementine + Sodiation TVB 10-7-M (27) 1/2+000/ N2 (a) (2+m) (2 8 5000 2000 2000 5000 2000\_\_\_ 1000 1000 200 7.00 200 plated Cell in digh 5.5 for then add diving pump I har after pump with chamber put incuabtor 24 hr ofic incusiotor. then ratiation 17:19: from 11/3 point -0.02 ml +1.95 mi =10-5\_ jul +9 ml = 10-6. Hataunt mean 55 57 N2+0, of Count SF Inem GZ.183.169. 168 8.0034 6.007 63 Bit 60.79.65 2-4-189-221 704.7 0.102 0.042 0.082 126 24.170.220 210.3 254 226 226 235.3 0.47 6.21 Est 15.113.99 104 0.67 (PE) 130. 129. 145 134.7 0.51 (PE) \_ c 99. 98.108 101.7 102 Count C2+2ref Count 0.06 6.087 0.046 Ect 50.45.60 121.121.120 120.7 51.7 1.27 196. 167-191 184.7 0.035 0.16 64 72.71.70 71 0.43 0.63 216.7 21/ 216 223 46y 42.56.53 50.3 c.69 (PE) 137.3 129.148.135 · 0.225 (PE) 45 , 49. UH. 42

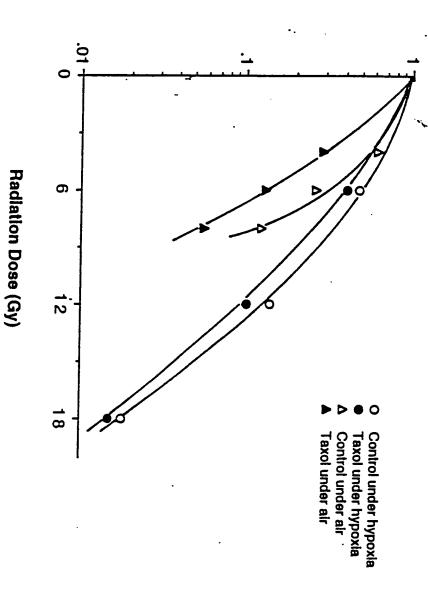
# Radiosensitizing Effects of Nitro-phenyl-taxol (100 nM) on CHO Cells



						T=10-8		, p
_ Taxof + Rad	ation_	44P01	C RT 07	c+b.2.3	ين .	ric		
- Hyporictorus			· - · · · · · · · · · · · · · · · · · ·			ee		
70000				7 <i>000</i>	100	.0		~
5000				fort	50	0	·	
1000			.4	200	20			
posted cell in	Int his		to then	aid druly pu	mp / hr. a	Her pump wit	h chamber	•
incuiator 24 lm	ath Fin	disting	edic in	inclibator.		·		
Druf: from 7		0.5 ml 1	-49.5 ml =1	o-5-				
Druf: from 7	2101 10	V	(media) 500 m (=10	. 6			ot)	
		_	SF/pc	N'2 Const	nl ean	SF	SF/PE	
NE = Dr. of Count	125	0.00b	0.015	105.130.40	108.3	0.01	0.018	
G 178.110.127	220.3	الله ٥٠٥	0./02	174.161.172	169	0.085	0.143	
04-28.201.197	173.7	0.174	o.404	148.101.137	142	0.284	0.481	
C+ 49.178.194	85.7		(PE)					-
85.102.70			•	Dr Count				<u> </u>
62+ Proficement	34.3	0.007	0.057	146.161.148	151.7	0.076	0.124	
\$ W. 26. 32	32	0.016	0.133	172.159.154	161.7	0.162	0.265	+
4 79. 35. 22	<del></del>	0.035	0.289	191. 186.194	140.3	0.381	0.624	
6f 38. 39. 27	24.3	0.12(	PE)	119. 116. 133	122.7	0.61 (PE)		
7 26.18.29								-
								-
					<b>b</b> .			
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## Surviving Fraction

## Radiosensitizing Effects of Taxol (5 μM) on CHO Cells

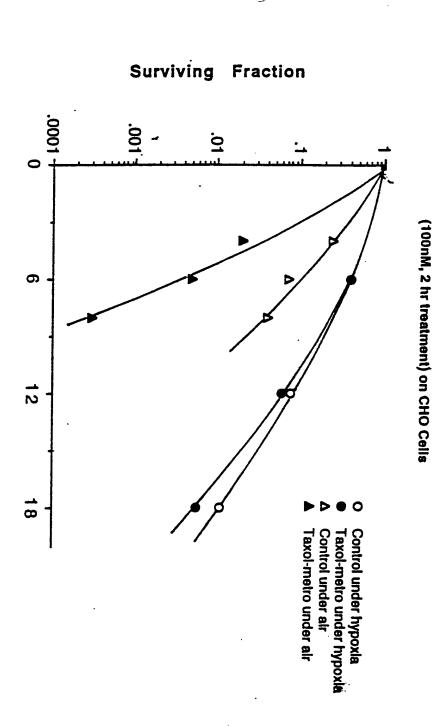


-				
	·		3:4 = 2.1-14	
SC PLUI	z Exferiment		KT=307	
	. <del></del> .		The second secon	
be +RI_2600	NET+Druz Zecu	zlar prof 200	and the second s	•
///	ש ססטו אמוצח ב-סס			
		(1) / 1) / 1) / 1/7		
W R7 500 EM	A sus 2 days 1	ter (total redish) take	3 dishes add drug 7 dishes	
phated cells each a	11 7×100 3640 14	dief. 3 dich Nodry. PH.	t inculator. 2hr. 4hr. 6hr.	
8 64 ofic radiation 4	After RT. 300711 asa	a la V		
jepsin then plated co	ell in dish incubator	Touch has been	w1	
<b>1</b>		D/ vg: from 100 m	11. I PALSE LUGA RAM	
		9.02 m (+ 5. pm)	0+2me old Medium. total.	
			2.5.	
Court mean	3F 3F/3E.		*.	
	0.61 1.83			
2 hw 12 122 · 118.15. 121.7	0.635 0.87			
Wp 124. 113.134. 127	6.65 0.89			-
WD 179.184.129 130.7				
2 154.136.147. 105.7	0.73(PE)			
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				501= /MM	1
50 and Metor Toxic				502=0.1mx	1
N2 22	N <sub>2</sub>	0z zdishos		503= 0.01 mr	1
3dishus 3dishus	Mi 3diffet			Mi=Metal 20	
	147 4			Mz=Metor 10	
	M3 "		المراكب والما	Mz=Metor 1 "	M
pated cell in dish incubator	3.5 hr. then add	drug ofic and	HAPONIC	had add	ul.
The same of the sa	7.0	•			
17010 pm f many 7 days	brig from. 50	100ml -> 0.2ml	+198=/1	·M .	
redium inculation 7 days.	orey in the	<u> </u>	18me = 0./ r	nM.	
metor: 136	mg/40 me H1355 =	3 1	10 .		
	· 1/	2ml.	+18ml=0.0		
	wt+10mt = 10 m				
2	me+18ml=1mm	· · · · · · · · · · · · · · · · · · ·			ce/.
	SF 57/0E	V2 Count	mean	SF	SFPE
N2 Count In Em	<del></del>	0 0 0			
nM 50, 200	v.65 1.137	133.116.138	129	v. 645	4008
MM 362 124.141 1	0.64 L/23	129.145.137	137	0.685	10/
0 mm 50 128.127.129 128	0.57 (PE)				4.0
0 Control 115. 112.114 113.7	0.545 0.46	130.146.103	126.3	0.63	o-99
20MM M 117. 99. 111 109	0.54 1.03	136.133.125	131.3	<u>c.ble</u>	1.026
CMM M2 128. 107.118 11/1/	•	133.145.128	135.3	0.68	1.057
1 mM M3 96.135.123 118	0.59 1.035				
	<del>.</del>				
	<u></u>	•	ķ		
	:	<u> </u>			· .
					•

Taxol-line	tor + Rad	iation	CHO C	થા	Drig =	= 10-7
N2+0rv		Az	RT (GY)	Oz+Orif	O2	
29.000		10.000	8	5000	2000	· · · · · · · · · · · · · · · · · · ·
		2000	6 -	2000	500	
2000 500		500	4	1000	700	
		700	0	200	200	
200	rd 2 has	1 1.40	then ad	dough ofic in	newbotor. hypoxi	c pump /hm.
ME CELL M	dian your	A 272 1	hr hien	polistion after wi	esh out therdrif.	put new
of purp foot	· valor	1. Low Chica	1		,	
tium incubato	7 7 day 1	ALLY - 77 IOSA				
enf from: 10	,,,	-5 0 4	1+7,2~	=10-6 ->8~2+72h	1=10-7	
zorel t	1.98 ml=/4 14255	-> 6-8		2701 171		
						SF SFE
N- Count	mean	SF		16d 101 79 22	67.3	c.003 0.0057
49.61.85	65	9.0065	0.011	180 101.79.22	84	0.042 0.071
113.94.83	46.7	0.048	0.078	100.79.73	128.3	0.26 0.435
119.130.119	122.)	9.25	p.40	136.108.141	118.7	0.59 (PE)
132.127.112	123-7	0.62 (PE	) <u> </u>	125.128.103		0.31
2 count			:	02+Drug	4.7	0.0000 6 0.0003
51.56.63	56.7	0.078	0.04	0.1.0	0.3	0.00/ 0.005
30.17.30	25.7	0.05	0.072	3.0.4.	. 2.3	0.0047 0.02
38.25.44	<u> 35.7</u>	0.18	0-25	8.3.3	47	
153.132.141	142	0.71 (P	<u> </u>	48.36.47	43.7	0.22 (PE)
_			<u> </u>			
			!		· · · · · · · · · · · · · · · · · · ·	
			!			

Radiosensitizing Effects of Taxoi-metro



Radiation Dose (Gy)

左 7

50	PLOR EXPE	i'ment			RT=864	
. Cell					proj=0.1 m14.	
1 h/ RT 20.00				•		
1/427 10.60	- aby+OT+ DW	9 10.000	zhr ORT+Drif Zo	0		
INTRT Seco	Ulm+RT+ Dru	7 5000 -	4hr ORT+Druf 20	0		
W+RT 2000		\$ 2000	blmorttong zo	6		<b></b>
MINI						
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						+

			<u> </u>		
5 c and M N2 02 C1 3dish 3dish	etro toxicity	CHO CEUS.			
N2 02	No Mi 2dish	02 21:4	5c1	= 1mm	Mr = Zomy
C2 "	M2- ·			= 0.1 mM	M2 = 10 mm
<u> </u>	1	ar In	5C 3	= 0.0/mm	Mzzlmm
Plated Call in dish.	each dish put	200 ceils in incent	alor 3 lm	then a	ld drug
pump I'm after pump.	pm water buth 3	7 c 1hr. then We	ash off	the drug.	add new
medium incubator	8 dows . Then Stain	1. Count			·
	·	Dri	y: metro	136 mg	=0.1369
Truf: 50 from women.	-I-m· each dis	hadd z.5ml.		<u>+40 m² = 2</u> (HB\$\$)	
7-1+18-1=0.1			-	(HB\$5) <del>10~(=10+</del>	
74/8h = 0.0	•		V	\$ ~ = 1 im N	
(HBSS)	!		20-(+)		
Nz Court mean	SF SF/PE	Oz Court	Mean	SF	55/02
Ct 0		0			
Cz 129.108.104 113.7	0.57 0.848	121,134.140	137.7	0.66	1.062
Cz 147. 12/. 109 125.7	0.63 0.938	129.138.117	128	0.64	1.032
0 142.129.13/ 134	0.67 CPE)	143.118.112	124.3	o.tz(PE	)
4. 122. 134.129 128.3	0.64 0.958	136.130.122	12.9	0.65	1.043
12 130. 125. 127 127.3	0.64 0.950	130.124.120	124.7	0.62	1.005
M3 133. 130. 119 127.3	0.64 0.950	120.126.109	118:3	0.59	0.954
		<u> </u>	<b>\</b> .		

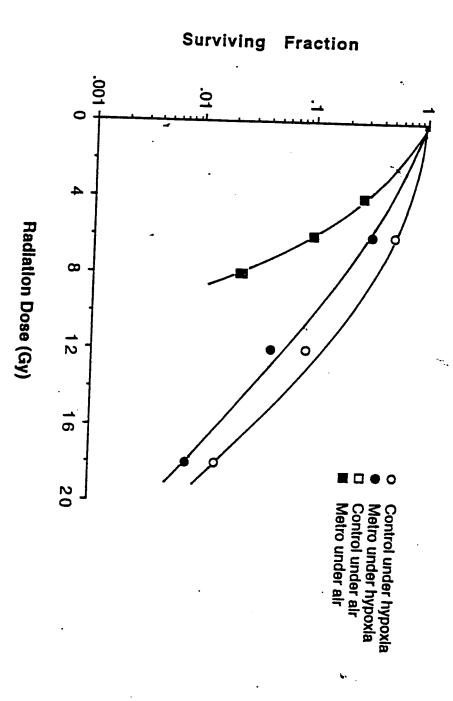
5	C PLDR	Experi	ment.			5c=0.1mM		
OW RT						RT=861		
a Control				-		•		
	5000	2/WRT+D	5,000 -	· Zlm D	260			
	5000	UlW RT+U		4hr0	200			
lar RT	2000	6WRT+D	!	· blw	200	***		
		•						
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Nitro-phonyl-car	ol (TNB.	T Radi	ation	CHO Cell			rug=10-7
) N2+D	NZ	RT.		0	)		
70.000	10.000		10.000	500	77		
. 2000	1000	6	5000	1000	2		
1000	500	4	-2000	500	?		
200	200	0	200	200			<del></del>
pated cell in diff	incubator	3/m the	n ádd di	rug pump ilm.	after p	not waterbat	4 37°c im
her radiation ofic	in incubator	<u> </u>					
cuf Hom 1NB 10-3 (1	mm) -> 0.02	m+1.98m=	:10				
7		+9 W=10		<u> </u>			
	gn.	+72 W=10-7					
N2+0 Court	riean	SF	STPE	Na Court	mean	9F	SF/PE
- 179. 95. 99	u	0.0056	.0135	64.78.36	5-9.3	0.0059	0.0138
6f 105. 110. 110	108.3	0.654 0	./3	84.26.52	54	0.054	0.13
A 124. 164. 155	151	0.151 0	.368	72.71.60	67.7	0.135	0,3]
85. 97.54	82	0.41 (PE)		110.94.55	86.3	0.43 (PE	)
Oz + O Count			<u>.                                 </u>	02 Court			
74.80.73	52.3	0.005	9 دن.	42.59.61	54	0.0/08	0.018
1 148.135.130	137.7	_	· <i>9</i> 47	37.54.33	41.3	0.041	0.07
f 171.157.18Z	170	0.085	! :/ <b>S</b>	64.80.78	74	0.148	0.25
112.110.117	113	0.565 (PE)		109.120.126	118.3	0.59 (P.	<u> </u>
							<del></del>
	•						
				·	<b>4.</b> ·		
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	  -	prof = 0.1 mM RT = 864
50 PLDR Experime	al	RTSOF
		•
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	·	N. Committee of the com
	· ·	
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		N

	Metro	+ Radiati	on				Ore	of=0.5 mm.
RT 64) — —	_N2+0		Nz	RT.	02+12		0z	
<i>y</i>	20,000	10.	000	8	10.000		000	
2	2000	10	00	6	2000	10	700	
, ,	500	Zu	0	4.	1000		00	
9	200	20	טפ	Ó	200	7	.00	
a hot a	1 colls in	dish incus	nator alm	Hun	add drift pur	P Ilm. H	lien waterbu	th 37° 1 m.
lle see	valiation ori	ic in incular	tor after	Valiation	Wash of the	drug add	new men	liam inculstar &
_gacu Drcd·	martor. 6.8	Grand / Count	(URCS) PAG	le digh	3 me doct.			
•		mean	SF	/	V2 Court	111 <i>04</i> n	SF	STORE
	12+0 Court	b7	0.0034	0.008		66.3	0.0066	0.015
•	15.60.46	3/4.3	0.014	a.045		4/	0.041	0.093
	b. 28.41			•	37.54.47	46	0.23	0.523
¥	16.70.74	71.3	0.143	1	fo. 63.10]	88	0.44(PE	~
	4.46.30	86.7	0.43 (PE)	<u> </u>	62 Court	- 00	<u> </u>	
•	2+DCount					69.7	0.711	0.024
٠,	5. 124.123	120.7	0.012	0.023	82.68.59	· · · · · · · · · · · · · · · · · · ·	0.014	0.(02
,	108.104	106.7	0.05}	0:/	57.63.55	<u>58.3</u>	0.058	0.275
F 137	1. 150. 152	146.3	0.146	0.274	42. 20.32	3/.3		
9 103	. 112.106	107	0.535 (PE)		118.106.119	114.3	0.57 (PE	<i>)</i>
				_		<u> </u>	<del></del> _	
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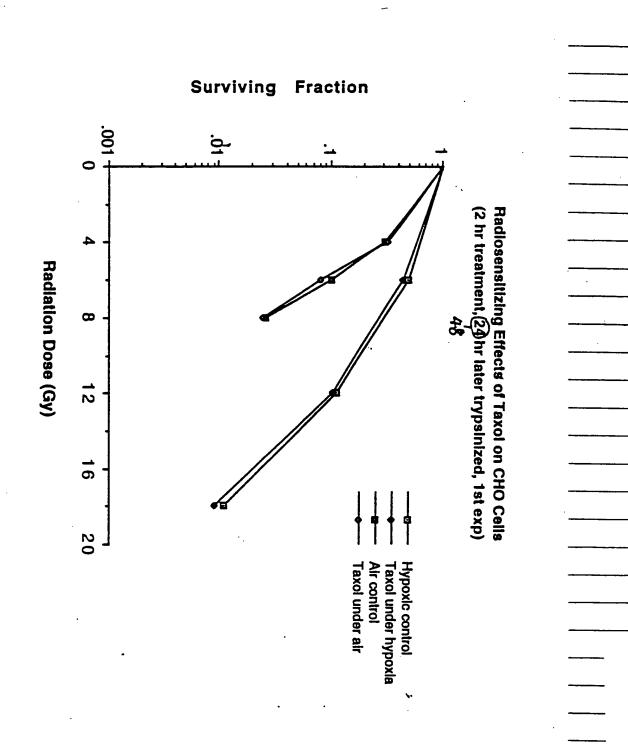


4.

	netro +R	adiation	(znd)	<u></u>			Drug =	8.5 mM.
RT YI	N2+D	Nr		RT GY)	02+0	Oz		
8 	20.000	10.000		8	10.000	5000		
12	2000	1000			2060	1000	· ·	
6	500	200		4	1000	200		
	200	200		0	200	200		
Dh.	ad Cell in dia	h in cubat	of 3hr.	them add	drug pump Ihr.	after pur	p put wat	exputh 37 c
ב <del>יבות ן</del> מול <i>ו</i>	ther vadidio	r. ofic i	vork in in	cubated .	Ater rediction with	h of the d	rif add n	ew medium
	whater 7 day			•				
	of: Metro 6.		HB65.					
	No +O Court	h1can	SF	58/05	Ne Court	Mean	SF	· 5F/pE
864		32.7	0.0016	v.oof	37.46.26	36.3	0.0036	0.008
•	49.50.65	54.7	0.027	0.069	bb 67.60	64.3	0.064	0.147
66/2	123.122.120	14.7	0.243	0.611	43.84.56	61	0.305	0.698
.E.J	57. 48. 84	79.7	0.398 (P	E)	70.74.113	87.3	0.437(8	E)
	OztD Count			:	Oz Count			
861	132.134.102	122.7	0.012	0.016	62.64.64	63.3	0.013	0.017
600	104. 124. 45	14.3	0.057	0.076	61.79.56	65.3	0.065	0.087
46	187. 204. 149	180	0.18	0.24	52.42.59	51	0.255	0.334
-T- J-	141. 138. 171	150	a.75 U	アモ)!	146.153.152	1503	0.752(	PE)
	711 1.0 1.71							
							•	
<del>-</del> -								

Radiosensitizing Effects of Metronidazole (0.5mM) on CHO Cells (2nd) Surviving . 01 Radiation Dose (Gy) œ 12 16 Control under hypoxia Metro under hypoxia Control under air Metro under air 20

	مالم د	allo Ca	L iveatures	t 48 hr later	typsiniz	ed expan	rest
	1501016 .		exid on	e day later one	2 dith a	4 5 fle	EL THU
. 1 1-00 - 1		124 4716	MICO 2h	w 37, 3/C MCME	THIS	_ www_ 1.1	_ MALLEY TA
- to and solling !	. Sucker	re huc	then 11/19	singe from park	CEIIOM Q	con nouse	The two
Thours. then Impor	ic Im o	Tic xu	in treuba	tor. then issal	iste affa	Vadietim	Pick in
in whater 7 days /	ater stain	Court					
KT Nation	Not 1	B55 (Cg	y 62+Tar	1 C2+HB		of: from 10	(1007)
18 10,000	10,	<u>8</u>	2000	7000	<b>-</b>	fatol (H	(a)
12 2000		00 6		500		3.05-4+9.45	1=10ml.
6 500		,0 4		200		DAISE HEST	
0 200		0 0	SFF	N2 + HB Count	Mean	SF	SF/PE
N2 +0 Count	jusan - a		0.009	73.87.92	84	0.084	0.01/
1869 61.45.71	<u>59</u> 132.7	0.066	•	165. 18.172	174.3	0.087	0.113
1269 124. 159. 115	138	0.276		174. 191.193	186	0.372	0.482
66 150.174.130	127	0.635		160.56.147	154.3	0.772 (	PE)
0 137. 120. 124 02+D Count			:	02+HB55 Com	t		
864 30.35.20	28.3	0.014	1.075	40.44.41	41.7	8.02/	0.026
601 62.36.39	45.7	0.046	0.08	89. 74. 75	<u> 79.3</u>	0.074	· ·
46 83. 92.98	91	0.182	a. 318	116.117.124	119.	0.238	E
0 14.114.116	114.7	0573 (	PE	180-164-153	. 158	0.74 (PE	
						· · · · · · · · · · · · · · · · · · ·	
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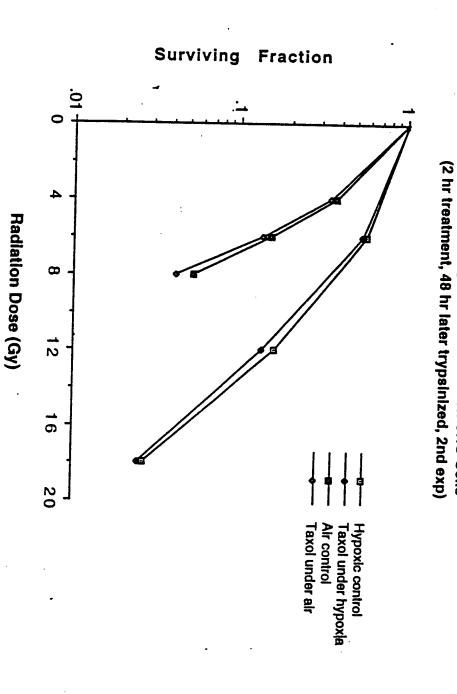


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in

Repeat	Experiment No + HBSS	RT (61) 62+P	Oz fH	855	_ dong:	trantocol.
N2+0	10.000		200	<u> </u>		10-3 (mM)
10.000	2000	6 1000	1000	·	1.0500	+ 9.95 m =5x10-6
500	500	4 500	. 500	0	<u> </u>	•
	700	0 200	20	0	DM3-2	H85
700		SF STOR	NaCount	ni ean	SF	SF/PE
N2+TMALC	108	0.0108 0.025	168.186.159	171	0.0171	0.027
112.125.87		0.059 0.137	197. 209. 210	26.3	0./03	0.161
127.119.107		0.229 0.533	187. 173.183	181	0.362	0.568
124. 108. 112	86.3	0.43 (PE)	115.122.145	127.3	0.637 (1	OE)
77.88.94			02 Count	•		
P2+P Connel	36	0.018 8041	78.82.52	70.7	01035	0.052
7 23.34.41	60.7	6.061 0.138	106.103.99	102.7	0.103	0.152
1 59.58.KS	75.3	0.151 0.342	_	12513	0.251	0.371
\$8.86.92	88.7	e.al (PE)	126.14/-138	135	0.675 (	PE)
88.86.72	80.7					
	·					
		:		May 1		
						<u>.</u> .

Radiosensitizing Effects of Taxol on CHO Cells



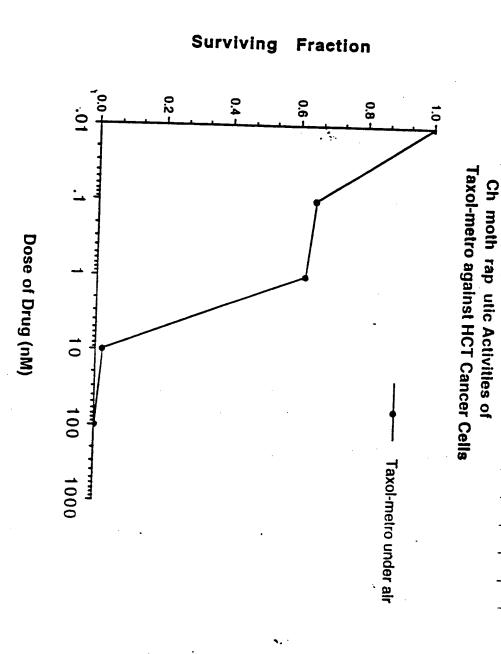
•/ 1)

- Total . T-B on HCT cells - 7	tolicity	
1-5-3 dishes 0 22 men		
1-6 "	<u></u>	_
1-7 , , , , ,		
F-8 1 2.0.0.		
1-B-5 · 000		
C-8-6 , 200		
~B-7 , 000	·	
(-13-8 , 1.00		
0 - 69.66.62 65.7 0.728 (PE)		
		<u> </u>
plat cell in dish incubator for the	to 1 sof	
the dring put new medium Are lays &	T. N. p.	— . -
ory Total from 10-3 (1mm)	-5	
	dich all os = +3 = 10  (old)  dish add os = 6	<u> </u>
6.2 + 1.8 = 7 × 10 Pach (H\$35)	-7	1
0.2 -1.8 - = 7×10-7	4 fish all 1.5 me +3 me = 10	<del>-</del> .
0.2 m + 1.3 m = 7×10 8 cack	dish all 15-4+3-4=10	— <u>;</u>
\$-2×+ No. 1 = 1/A =		—. <del>;</del>
1-B from 103 (1mg)		<del>_</del> ,.
4.18+2.39 W= 7x10 5 each a	dish add 05m(+3-1=10"	— ;
0.2 m + 1.8 m = 7×10 6 each a	dish add asme+3-e=10"	`
		—, y
		— : <b>;</b>
	•	

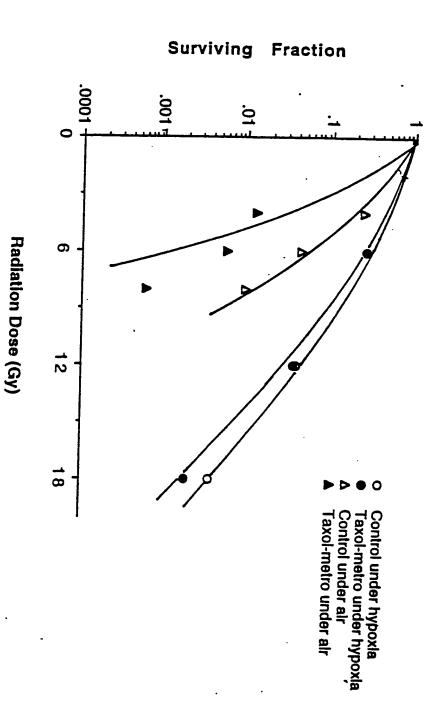
Nitro-p	hemyl-t	exol + Radio	ation on cHo	ce1/5		[NB=107	
f; N2+D	<u> N2</u>		t, C2+D -	Oz.			
201000	10.000	8	5000	Zeoo	<u>.</u>		
5000	7060	6	- 2000	1000			
1000	500	4	1000	500			
200	200	<u> </u>	7 Zoo	200	•		· ·
plant ceil in	dish inc	wholor for	6/18. then add	I don't pump	Ilm. after	prop with	
Charabar put		24.29					
new medium in						<i>,</i>	
Drug = TNB /mi						70.00	
		m+91=10-6					-
		0 + 40 M = 10				•••	1
N=+0 Count		SF 57		mean	5F	SF/SE	
864 88.89.83	86.7	soct or			6.0076	0.014	
16/ 206. 177. 207	196-7	0.039 0.0		_	0.077	0.142	
by 243. 245. 199	229	0.229 0.4			0.578	0.7	
109. 100. 85	98	0.49 (PE)	102. 123.10		0.54 (12	-	
02+0 Court			02 Count				
1 51.50.74	58.3	0.92 0.01			0.062	0.097	
\$ 60.70.73	67.7	0.0338 0.13			0.204	0.32/	
70.74.79	74.3	0.074 0.2			0.377	0.592	
53.47.53	51	0.255(PE)		132 127.3	0.637	•	r uni
		i	1)2, 110.3				
		:		<b>~</b> , ·	-		
•		:				•	A STATE OF THE STA
•				······································			1

	Taxol	and Total-B	Toticity on	e HCT	cells.	· · · · · · · · · · · · · · · · · · ·	
T=Takel	Plant ced	L-	TM01-B.	plant ceds	Court		
7-10-6	500	0	T-B-10-6	500	0		
1-10-7	500	1.00	1-15-10-7	500	1.00		
T-10-8	500	2,3.1	T-B-10 t	500	0.0.1		
T-10-9	500	1900	7-8-107	500	(.1.1		
7-1010	500	5.0.2	7-B-107°	500	/. 2./		
Control	: 200	150.150.152					
plan	t HCT C	BUIS in dish, each	dish 500 ce	14. Contro	1 zoc cells. inco	hator S.Shr later	
ald	o. 5 ml dru	1. total 3.5 m ex	ch dich drug	in medium	n. then keep in	whator zellers. with	
drul	later W	ash off the drug	I all new	nedium h	cep incubater f	or adays. stain.	
		7/			f		
DVIS:	Hom: Tor	101 . Taxs1-B. 1	10-3 (Imm)				
	<del></del>	12 mt + 1.59 ml = 7 × 1	5				
		·	<b>\</b>				
		V 1985	b each dish	add 0.5	we with dish m	edium 3m. total 3.54)	
		2-4-18-4-7X-0	.7	(dru	<i>})</i>	=10	
	C	2m+1.8m=7x10	i				,
	.0	-24+1.EW=7X10	9		•		
		<i>V</i>	10				
	•	20x + 18xx = 7x10				``	
			į		<b>~.</b> ·		<u>,                                    </u>
	· · · · · · · · · · · · · · · · · · ·	•					
	•		:				
				-			
	•					منور مد	

T-M and TNB in HET cen toxicity	
C-M cens count mean SF SF/PE-	
EM 107 500 0	er en
I-M 10-8 500 10.\$.6 6.7 0.013 0.019	
7-M 60-9 500 212, 25.197 24.7 0.429 0.609	
7-M10-10 500 221.222.243 228.7 0.457 0.649	
[NB 10] 500 000	
TUB10-8 500 7.5.6 6 0.012 0.017	
TNB10-9 500 174.25.160 183 0.366 0.519	
TNB10-10 500 187.189.178 184.7 0.369 0.524	•
121 M3. 1F 141 9.70 (PE)	'
prant 500 Hot cells each dish in incubator for the than add druf with	meauna.
- feet in inculator 24 hrs. later useh of the drug. add new madhum inculator kelp	107
adays stain.	
Drug from 10-3 (Imm)	
11 M + 9.95 ml =1.1×10-6 = each dish add 0.3ml + 3ml = 10-7 (ord medium)	
JH655	<u> </u>
0.2~(+1.8~(=1.1×10-)	-,4
0-2-4+1.8-e=1.1×10-8	
V -/1 X10-9	
6.21-41.6	
	-



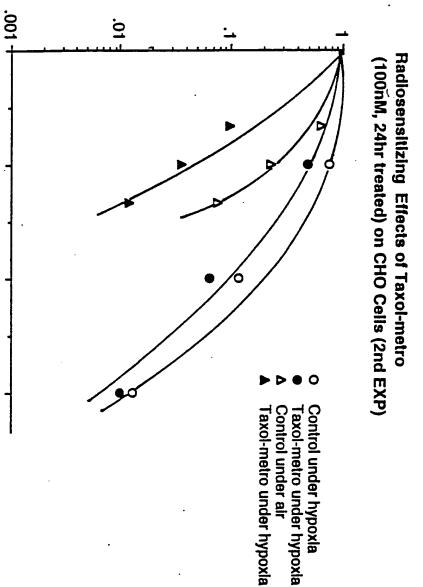
	Total-Metro	+ Radia	tion (Rep.	eat Ph	eriment)	D = 10	
RT	NztD	Nz	0210		000		
et	20.000	10.000	Hy 5000	5	оv		_ :
04	2000	7 000	tof 1000		200		
of	500	500	<del></del>		200	19 32	
0	t colo cells in	780	tal box 3h	. then add	drug wir	th H1355 pur	p Ihr.
P/ant	in inculator.	diffe inclin	P but water	Just 187 C/M. 1	hen iwah	ate off	et. Wath
dic	in inculartor. he drug add r	aprer p	les a mark	ator sdufs.	stain.		
<i>34</i> €	he drug and r	12 10-3 (	(marl)	J			
Drug:	: from T-M . T.	NB 10 -1-	-5				
	- Toak th	9 km2 = 10 855					
	0-8-(+)	7.200=10	•				
	84+72	- = 10 7				<i>CT</i>	5Ffre
	Nato Court	mem	57- 57/08	Nacount	mem	57	0.004
N.S.	27. 20. 2	22.7	0.001 0.002		74.7	010015	0.04)
1264	41.4.48	43.3	0.022 0.037	57.58.44	53	0.0265	0.264
for	84. 88. 62	78	0.156 0.27	1df. 74 77	<u>&amp;</u>	0.643 (PE)	· .
	111.120.116	115.7	0578 (PE)	120.126.40	128.7		
	02+17 Count			D2 Court	11	0.0055	0.0/
864	1.00			12.9.12	127	0.025	0.045
64	1.1.2	1.3	0.0007 0.0		27.3	0.137	0.244
46	1.1.2	1.3		29.23.30 ) 118.104.115		0.56(12	.)
- <del></del>	18.23.21	20.7	0.103 (PE	) 10.104			
	_						•



Radiosensitizing Effects of Taxol-metro (100 nM, 2 hr treatment) on CHO Cells

大学の大学 17年 日本 日本 100 mm

 -/d	N2+0	Na	R.T.G.	1 02+0	113 (Refeat	Oz			<del>-</del>
	20.000	10.000		5000		900	·		-, -
	4000	7000	6:	2000		780			<b>-</b>
	1000	500	4	1000	5	60			·- ·-
		200	Ø	200		00	·\	11 11	
	nt Cell in d	ish incert	ator for	thes.	Hier add dr	ry with H	355 pump	1/m. 871C in	
								ladiation, often	
ncuba	which off the	brut zd	d new me	Lang Let	princulater -	for 8 days.	stain it.		
7-	from I-M.	W3 10	3 (1mm)			<u> </u>			·
Pruf:	your J-MI.	11/13/10	- 12-5						
	70,64	(+1.98 me	-6	:			7.66. HB55.		
		+7.200	=/ 0	esch	dish add 3.	e drug		<del>-</del> .	
		V +72-4=	7	STOR	NaCount	mean.	57	39/02	
	Noto Count	in ean	0.00275	71	56.48.31	45	0.0045	0.013	
6	35.45.55.	_15		0.064	86.109.58	84.3	0.42	0.118	<del>.</del>
64	57. 71.91	73		0.484	162.128.113	134.3	0.269	o.753	
4	81. 113.137.	110.3			62.80.72	71.3	0.357(P	£	
g	4. 6. H	46.7	0.228 (98		Or Court	mean	57-	SFIPE	
	Oct D Court	in ean	94	STIPE		£:3	0.043	0.077	<del>+</del>
62	2.5.3	3.3	0.0007	0-017	101.77.78		0.128	0.23	
Gf_	6.3.3.	4	8.002	0.036	123 · 125 · 137 156 · 190 · 18		0.355	0.638	
Hof	3.4.1	- 5.3	8.005	4.097			0.557		;
0	16.6.11	ll .	0,055	(PE)	124.110.1	00 ",")			
					<del></del>	<del></del>			
				_ <del> </del>					



Fraction

Surviving

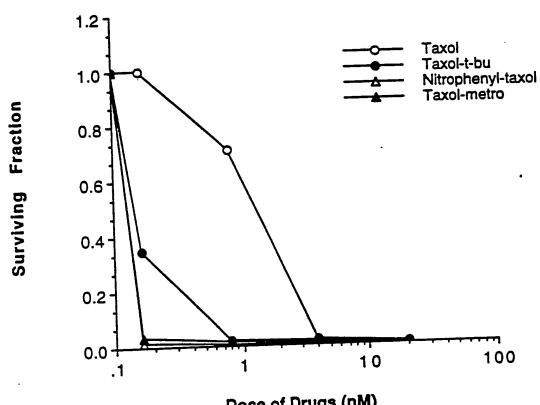
Radiation Dose (Gy)

O

		<del></del>		Drug=	10-9	
TOXOL+RT O	m Het cell	RT	0210	02		
NZ+2	N2		70,00	20.000		
20,000	76.000	307_		10.000		
10.000	10.000	667 -	5000	5000		
500	5000	46		200	١	
	200	<u> </u>	700		n lhr. He	( pump.
ruf Hot call in de	the inculator	for this.	then add drug	Milled J. Coulled	c ~ cod	Her Hart
						-
It the doubt add)	now modium sulp	in incurr	4 4 2 / 1 1	n if and Court		
8. 10901: 470m 10-3	1 ( ) ( 1 ( 1 ( 1 ( 1 ( 1 ( 1 ( 1 ( 1 ( 1	But (HBSS)=	1.14,0-6			١.
3. 1010 : 17000					9	
	. C. a	V 7. Z /- / / XI	o-8 each dish ac	U 1.5-4-43-	10-1 -dim)	
		c 51/pc	Netout	men	5 <u>-</u>	5//2
Nx+7 Court		'	v	o	J	<u> </u>
<u> </u>	<u> </u>	1002 0.0076	7.8.7	7.3	0.0027	0.00197
3.2.2.		007 0.022		48.7	0.0097	0.0262
42.35.78			74. 80.69	74.3	0.372 (9	E)
70.53.61	61.3 0.	307 (PZ)				
02 to Count			14.15.20	14.3	0.00082	0.0015
9.14.14		.0.06 0.00	•	105.7	0.0/06	9.019
75. to.54		.0063 0.0	A	zH.3	0.054	0.097
Z00. 187. 198		0.039 0.08	2 278.28/249		0.553	(PE)
A5. 79. 112	45.3	.477 (PE)	1.7.107.108	110 - 1		
				•••		
		i				•

[040]	Court	mean	. gF	stp=	
1 218	1.0.0	0.5	0.0025	0.0046	
T 4x0-9	4.1.1	2	0+01	0.0/85	
T \$210-10	81.74.76	77	0.385	0.71	
T 1.6410-10	107.11.118	112	1 0.56	1.0332	•••
Cand t-bu					
T-B zxie-8	1. 3	2	0.01	0.0185	
T-B 4X10-9	0.1.0	e-33	: 0.09)	0:003/	
T-B 8210	2.2.1	1.667	0.0083	0.0154	
T ~ 1.6 X10	43.35.35	37.7	0.1883	0.3425	
rand-Metro	ø				
F-M 2410-8	0.0.0	0			<u>-</u> .
T-M 4X10-9	1.2.1	1.33	9.00)	0.0/23	
T-M 8X10-10	2.4.4	3.3	0.d7	0.031	
T-M 1. 6x10-10	0.2.1	1	0.005	0.0092	
INB ZXIO-8	0.0.0	U	U	6	
TUB 4X10-9	0.0.1	0.3	0.0017	0.003	
TAB \$ X10-10	0.1.1	0.667	0.003	0.0062	
TNB 1.1410-10	2.1.1	1.33	0.007	0.0/23	
Control	100.11.114	108.3	0.542 (PZ	:)	
Plant HCT	cells in dish	incubator bhr.	then add d	rug with medium bey	in incubator for 24 hrs.
Usen wash	At the drup.	rdd new medium	n incolutor.	for adults. stain.	
	T-M. TNB from	7		12-1=4×10	
<del> </del>		- L	344	12m = 8 100-8	
		454=10 454=10-7 454=10-7	/	t 10	

Chemotherapeutic activities of Taxol, Taxol-t-bu, Nitrophenyl-taxol, and Taxol-metro on HCT116 Cells under air condition (1st exp)



Dose of Drugs (nM)

• •_	1-B=5x108				tion-	Radia	T Cell +	1-B on HC.	
٠.			02	Bt0			Nz	N2+D	<i>6</i> <u>}</u>
<b>`</b>			40,000	46.000	8	60	400	40000	}
٠.		·	10.000	10.000		<i>0</i> 00	20.	20.600	2
٠.			2000	2000	4	0	500	5000	6
٠.			Z00	200	6	0	20	700	0
<u>_</u>	water after	Stic in inca	samp Ihr.	then add drug	for blos.	bot N	dish inclu	at 141 cells in a	Plas
<u>L</u> _	the drug. add	russh off t	iation lotes	or exhits then you	all druf to	tal wi	23 hrs. to	p. put inculated :	bam l
				aunt.	stain. C	efs. the	of for 9d	medium inculator	n 2412
						<del>)</del>	·3(1mm)	4. from T-B 10-	11000
					6	1.150	2 -1 (HBS) =	11 w + 9 488	VI OJ
-ī						)			
		7	1 =5X10	add 0.3 ml + 31	sch dith	8		0.4+3.6 m	
_	STPE	97	filean	(druf) (old 1) Nz Loust		2 5F			<del></del>
	v.000Z	0.0000 \$17	3.7	6.3.2	0.099		8.67	N2+D Count	,6/4
•	0.00098	0.0005	10	14.8.8	0.00074			0. 1. 1.	1867
	0.015	0.0077	<i>38</i> .7	30.53.33	2 0027		1.3	/. 3. 0	126]
		0.51 (PE)	102	102.81.123		0.09		6.19.11	66}_
				oz comt	i	0.01	17.3	4 · 26 · 17	. C
	0.0007	1.1004	17.7					82+D Count	
	p. 0/8			71, 17. 15				•	80
	0.14}	0.013	113 16.	107.114.118				0	sof
_	V -14)		181	159. 192.189 114. 157. 128.					269
		· 63 (12	120.5	179. 171.14.				<b>t</b>	0
									No tip
			<del></del>						•
	<u> </u>								
					i				

DRUG: Taxol and TM 24 his prior Xray

umor : MTGBjtrented when seeme eine es dem

DMOI	i blien									ا ج	n m	<b>,</b>			•	
P:1					Date:		Tum				-	<u>- T</u>		0 1		<del></del>
roup	drug dose	radia	lia-	毕					4	5	4		8	9	10	"
		2,65-	_	1	9	105 -	10	9	8.5	8.0	7.5	6.0	7.5	8.0	8.0	4.0
Control	130 mg/	د عه . د		2	9	bina	9	9.5	4	7.5		7.5/	25	7.5	7.5	75
	/109	زحد.ه	16	3	9-19	10224-	10.5	10	9.5	9.5	3.9	9.0	9.0	9.0	9.0	9,1
206.4	100:-3/	مرد ره	15	1	- 6 00 00	10,5	9 -	9	28	8.5		7.5 8.0	7.5	7.5°	75	7.
2264	/FJ	0.55~	/2	1	PAM	101	4.5	9	8.5			7.5	75	7.5	7.5 7.5	7.5
1000		رح- ، ن		2	9-	ساور	9	8.4	10	8.0					MO	15.0
22 614 Constr	hi	1		1	9-4	10		11	11	<b>A.</b> 6	10.5		12.0	13.0	~2.V	12.5
RTA				3		9-	9.5	10	1015	10.0	10.5	9.5	9.5	9.5	10	1//
1 -			┡	4	<del> </del>	9	9.5	9.5	10	10.0	105	10.5	11.0	13.6	13.0	13.0
		<del>}</del>	$\vdash$	5		9	4.5	10	10	10.5	111.5	11.0	12	13.0	14.0	15.0
			<del> </del>	6		9.	15	7.5	105	10.5	11.0	12	12	13.0	140	15.0
TM Control	100 10	S.O.De	16	4	75 m		4.5	9.	85			7.0	7.0	7.0	7.5	7.5
I wi power of	ise They	1	<del> </del>	4	7.500		9.5	8.5		70	65	6.5	6.5	6.0	60	dreit
	i	9.31	16		T	1	9.5	18.5	8	FE	X	$\boxtimes$	<b>&gt;</b> <	$1 \ge$	1->	1-1-1
- 41	!	3.053,00		14	7.500	950		125	19	19.0	18.5	8.5	8.5	8.5	8.5	8.5
TM + 2264	100 1/49	سرراه. -11 و		سينسي	┼	47	9,1		9.5			7,5	スロ	7.0	7.0	7.5
		b=	418		<b>-</b>	911	91	12.5	8	17.5	7,5	7.0	7. 0	7.0	17.0	7.0
	/!	0.06				ã	2019	8.5	8	8.0	7.0	000	$4 \ge$			1 > 1
Tax:1 + 1267		: 6.013-			Ť	4-	10. 27	10.	111	11.0	11.5	12.0	13	14,0	140	14.0
		مرکن.و				1	10.5	10	dea	d>	$\propto$	$\geq$			1~	1
		0.053				4	1834	19.5	9	8.5	8.0	7-5			dead	4
		0.057	117	. 5	1	4-	10	10	7.5			7.0		dea	_	1
	į		416	: Þ		19-	المربو				7.5	1		-1		7
Taxo   Couty	ma - lk	7 1 0.057	Ar	7:		9-		8,5	8	8.0	7.5				<del></del> -	
TANO / Coutto		0.65	415	5_2		7-		8.	<u> </u>	7.5	7.5		65			
	<u> </u>	ځه. ن	715	<u>5</u>		9.~		8	8	7.5	7.0		_			1
		100	44	7 4	+	8	9.0.	-	8.			7.5		dead	71	
Toxal Contra	1	20 - 10 S	44/	5 5		18		<del></del>	8	7.5		6.5			doa	<u> </u>
		30.00	<u> </u>	5, 6		4	1.		19	10,8				<i>ਜ</i> ਼	14	140
Control			1	1		8		9	1/0	, 12.	0 12.0	13,0	14	15	15	15.0
Comercia			ţ	3	+	165				11.0	12.0	13.6		14	1/4	14
		Ì	į	-य		A P	6	8	19		111.0			14	15	15
			1	5			7.5	19	1.11			0 13 c			-	
_				6			6.5	17.	F Q.	0 10	1114	0 112.	5 13	1/4	5 16	1'2
		i	$\top$	Ť,	1.			i	1				1-		_}	_
To 09! 30	7		1	12		+										-
20::0					_			i.								+
	!	}	1	3				-		i	_ [	1				

10:39

DRUG :

Investigator:

P:2 Date: Tumor size in mm

Y:2-				Date:		107	n 0 f	212	، ح	, , , ,					•
Group	druq dose	radialia- olose	铲	92	13	14	15	16	17	18	19	28	21	22	23
TM		7.	-	10.5	11:5		130	14.0	145	145	dead	X	X	又	又
A Control	ŀ		2	<u> 7.5</u>	7.5	17.5	7.5	7.5	7.5	7.5	3.0		12.00	9.0	9.5
B TM + 226/			<u> </u>	- 9.5°	7.5	7.5	11.5	7.5	7.5	7.5	7.5	14. 7.6	75	7.5	16.0
			9	7.5	7.5	7.5	8.0	8.0	8.0	9.0	9.0	4.0	9.5	16:0	7.5
RT			3	7.5	7.5	7.5	7.5	8.0			8.0	8.0	9,0	0.0	10.0
C 2264 RT Control			1	16	16	17.0	17.0	17.0		18.9			See		-
C 4×1			2	12.5	13	13.0	14.0	14.0	14.0	15.	16.0	16.0	17.0	541	
Can ( ) a /		\$	3	11		12.0	122	130	130	13.0	13.0	13.0	3.0	13.00	14.0
	}		4	13 is	14 de.d	14.0	14.0	BU	140	14,0	15.0	16.0	dead	<u> </u>	-
			6	15		dead	-				-		· ·		-
DIM			4	2.5		8.0	<del>!</del>	100	80	90	(120	11.0	/2.0	12"	130
Cowlifol		į	2			0.0	1	0.0	9.5	713.	140	///	12.0	12	1/2
Lawira	İ		3				<u></u>			·					
< TM + 2264	<u>.                                    </u>		4	9.0	9.00	10.5	12.0	13.0	13.0	14.0	16.0	17.0	drad	<u> </u>	
RT	•	!	5	7.5	7.0	7.0	7.0	8.0	8.0	8.0	8.0	8.0	8.0	6.1_	8.5
		<u> </u>	6	7.0	7.0	7.0	7.5	9.0	9.0	9,0	180	11.3	11.0	11.0	11.5
F TOX61 + 224		:	1					·							
RT			1	15	dead										
			3									<u> </u>			
		: <u> </u>	4												
:		; ;	6												
C			<u> </u>												
G TO101			2												
_ Control			3												
H TONOI			4			<u> </u>									
Control		<u>.</u>	5												
		<u> </u>		111	14	14	15	ا سرا	16	17	, 4	<del>'                                    </del>	١	<b>'</b>	<u> </u>
I rehicle		<u> </u>	1 2	14	14	<u>। प</u>		15	10	-'/-	18sa				-
vehicle Control			3	155	16 14	15	15	dead	·						
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17164 DRUG :

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